1225900

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September 15, 2004

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APPLICATION NUMBER: *60/562,384*
FILING DATE: *April 14, 2004*
RELATED PCT APPLICATION NUMBER: *PCT/US04/25026*

Certified by

Jon W Dudas

Acting Under Secretary of Commerce
for Intellectual Property
and Acting Director of the U.S.
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14230 U.S.PTO

PTO/SB/16 (01-04)
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PROVISIONAL APPLICATION FOR PATENT COVER SHEET

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53(c).

Express Mail Label No. EV 389270027 US

U.S.PTO 22273 60/502,384 041404

INVENTOR(S)

Given Name (first and middle [if any])	Family Name or Surname	Residence (City and either State or Foreign Country)
Dusan	Miljkovic	San Diego, CA
Jeff	Van Drunen	South Holland, IL
Zbigniew	Pietrzkowski	San Diego, CA

Additional inventors are being named on the 1 *separately numbered sheets attached hereto*

TITLE OF THE INVENTION (500 characters max)

Dietary Supplements for Metabolic Modulation

Direct all correspondence to: CORRESPONDENCE ADDRESS

[X] Customer Number: 34284

OR

[ ] Firm or Individual Name					
Address					
Address					
City		State		Zip	
Country		Telephone		Fax	

ENCLOSED APPLICATION PARTS *(check all that apply)*

[X] Specification *Number of Pages* 4
[ ] CD(s), Number
[ ] Drawing(s) *Number of Sheets*
[ ] Other (specify)
[ ] Application Data Sheet. See 37 CFR 1.76

METHOD OF PAYMENT OF FILING FEES FOR THIS PROVISIONAL APPLICATION FOR PATENT

[X] Applicant claims small entity status. See 37 CFR 1.27.
[ ] A check or money order is enclosed to cover the filing fees.
[X] The Director is hereby authorized to charge filing fees or credit any overpayment to Deposit Account Number: 502191
[ ] Payment by credit card. Form PTO-2038 is attached.

FILING FEE Amount ($): 80.00

The invention was made by an agency of the United States Government or under a contract with an agency of the United States Government.

[X] No.
[ ] Yes, the name of the U.S. Government agency and the Government contract number are:

Respectfully submitted,

SIGNATURE

TYPED or PRINTED NAME Martin Fessenmaier

Date 04/14/04

REGISTRATION NO. 46697 *(If appropriate)*

Docket Number: 100700.0034PRO

TELEPHONE 714-641-5100

USE ONLY FOR FILING A PROVISIONAL APPLICATION FOR PATENT

This collection of information is required by 37 CFR 1.51. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 8 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: **Mail Stop Provisional Application, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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PROVISIONAL APPLICATION COVER SHEET
Additional Page

PTO/SB/16 (08-03)
Approved for use through 07/31/2006. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Docket Number 100700.0034PRO

INVENTOR(S)/APPLICANT(S)		
Given Name (first and middle [if any])	Family or Surname	Residence (City and either State or Foreign Country)
John	Hunter	S. Holland, IL
Jovan	Hranisavljevic	Belgrade, Yugoslavia
Martin	Fessenmaier	Aliso Viejo, CA

Number 1 of 1

PTO/SB/17 (10-03)
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FEE TRANSMITTAL for FY 2004

Effective 10/01/2003. Patent fees are subject to annual revision.

[X] Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT ($) 80.00

Complete if Known	
Application Number	
Filing Date	April 14, 2004
First Named Inventor	Dusan Miljkovic
Examiner Name	
Art Unit	
Attorney Docket No.	100700.0034PRO

METHOD OF PAYMENT *(check all that apply)*

[ ] Check [ ] Credit card [ ] Money Order [ ] Other [ ] None

[X] Deposit Account:

Deposit Account Number: 502191

Deposit Account Name: Rutan & Tucker

The Director is authorized to: *(check all that apply)*

[X] Charge fee(s) indicated below [X] Credit any overpayments

[X] Charge any additional fee(s) or any underpayment of fee(s)

[ ] Charge fee(s) indicated below, except for the filing fee to the above-identified deposit account.

FEE CALCULATION

1. BASIC FILING FEE

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1001	770	2001	385	Utility filing fee	
1002	340	2002	170	Design filing fee	
1003	530	2003	265	Plant filing fee	
1004	770	2004	385	Reissue filing fee	
1005	160	2005	80	Provisional filing fee	80.00

SUBTOTAL (1) ($) 80.00

2. EXTRA CLAIM FEES FOR UTILITY AND REISSUE

	Extra Claims		Fee from below		Fee Paid
Total Claims		-20** =		X	=
Independent Claims		- 3** =		X	=
Multiple Dependent					=

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description
1202	18	2202	9	Claims in excess of 20
1201	86	2201	43	Independent claims in excess of 3
1203	290	2203	145	Multiple dependent claim, if not paid
1204	86	2204	43	** Reissue independent claims over original patent
1205	18	2205	9	** Reissue claims in excess of 20 and over original patent

SUBTOTAL (2) ($)

**or number previously paid, if greater; For Reissues, see above

FEE CALCULATION (continued)

3. ADDITIONAL FEES

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1051	130	2051	65	Surcharge - late filing fee or oath	
1052	50	2052	25	Surcharge - late provisional filing fee or cover sheet	
1053	130	1053	130	Non-English specification	
1812	2,520	1812	2,520	For filing a request for *ex parte* reexamination	
1804	920*	1804	920*	Requesting publication of SIR prior to Examiner action	
1805	1,840*	1805	1,840*	Requesting publication of SIR after Examiner action	
1251	110	2251	55	Extension for reply within first month	
1252	420	2252	210	Extension for reply within second month	
1253	950	2253	475	Extension for reply within third month	
1254	1,480	2254	740	Extension for reply within fourth month	
1255	2,010	2255	1,005	Extension for reply within fifth month	
1401	330	2401	165	Notice of Appeal	
1402	330	2402	165	Filing brief in support of an appeal	
1403	290	2403	145	Request for oral hearing	
1451	1,510	1451	1,510	Petition to institute a public use proceeding	
1452	110	2452	55	Petition to revive - unavoidable	
1453	1,330	2453	665	Petition to revive - unintentional	
1501	1,330	2501	665	Utility issue fee (or reissue)	
1502	480	2502	240	Design issue fee	
1503	640	2503	320	Plant issue fee	
1460	130	1460	130	Petitions to the Commissioner	
1807	50	1807	50	Processing fee under 37 CFR 1.17(q)	
1806	180	1806	180	Submission of Information Disclosure Stmt	
8021	40	8021	40	Recording each patent assignment per property (times number of properties)	
1809	770	2809	385	Filing a submission after final rejection (37 CFR 1.129(a))	
1810	770	2810	385	For each additional invention to be examined (37 CFR 1.129(b))	
1801	770	2801	385	Request for Continued Examination (RCE)	
1802	900	1802	900	Request for expedited examination of a design application	

Other fee (specify) _____

*Reduced by Basic Filing Fee Paid SUBTOTAL (3) ($)

SUBMITTED BY				(Complete *if applicable*)	
Name (Print/Type)	Martin Fessenmaier	Registration No. (Attorney/Agent)	46697	Telephone	714-641-5100
Signature				Date	April 14, 2004

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This collection of information is required by 37 CFR 1.17 and 1.27. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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DIETARY SUPPLEMENTS FOR METABOLIC MODULATION

Field of The Invention

Nutritional supplements.

Background of The Invention

Numerous nutritional supplements are known in the art, and most of them offer promise to modulate metabolism or even cure disease to at least some extent. For example, immune status is allegedly improved by various Echinacea extracts or zinc-containing compositions. In other examples, body fat is supposedly metabolized at an elevated rate to reduce weight. In still further known supplement compositions, amino acids, steroid-like molecules, etc. are advertised as being effective to increase muscle mass. However, such statements are typically not verified or endorsed by the FDA, and the efficacy for the advertised purpose is all or almost all of these supplements questionable.

Among supplements that have been shown effective to at least some degree are chromium compounds and food items containing such compounds to increase glucose utilization. However, numerous chromium-containing supplements exhibit significant toxicity (*e.g.*, Cr-picolinate) or have only relatively low solubility and/or bioavailability. Such difficulties may be even further compounded where chromium-containing supplements are combined with other nutritionally valuable compositions.

Similarly, phytosterols have been demonstrated to reduce serum cholesterol. However, biological effects of low-term administration is poorly understood. Moreover, such sterols need to be administered in relatively high quantities to be effective. Alternatively, serum cholesterol can be reduced by ingestion of barley or barley extracts, which typically contain beta-glucan at relatively high quantities. However, to achieve at least some cholesterol-reducing effect, such glucans need to be ingested at rather large amounts.

Therefore, while there are numerous dietary supplements known in the art, all or almost all of them suffer from one or more disadvantages. Consequently, there is still a need to provide

improved compositions for nutritional supplements, and especially those that modify the metabolism of a person.

Detailed Description

The inventors generally contemplate that numerous cytokinins and related compounds are incorporated into a dietary supplement or other food item to effectively modulate the metabolism of a person. Particularly preferred modulations include improving glucose utilization, treatment of type II diabetes, normalization of dyslipidemia (including hypertriglyceridemia and hypercholesterolemia), and treatment of syndrome X.

Especially preferred compounds and extracts are described in our co-pending provisional applications with the serial numbers 60/499,637 (filed 09/02/03), 60/493,447 (filed 08/08/03), PCT applications with the serial numbers PCT/US01/07527 (filed 03/08/01), PCT/US02/07199 (filed 03/08/02), and U.S. Application with the serial number 10/668,921 (filed 09/23/03), all of which are incorporated by reference herein. It should be appreciated that contemplated cytokinins and related compounds may be present in form of one or more pure compounds (*i.e.*, compounds having purity of at least 90%, more typically at least 95%), and/or as partially pure compounds (*i.e.*, compounds having purity of less than 90%). With respect to the related compound, it is generally preferred that such compounds will include a heterocyclic base (typically with purine or pyrimidine scaffold), and in particularly preferred aspects, the related compounds include acylated and/or acetylated nucleobases (*e.g.*, N-acetylguanine), which may further be substituted with a glycon (*e.g.*, N-acetylguanosine) or other group.

In still further contemplated aspects, it is preferred that at least one cytokinin in the dietary supplement or other food item is in biologically active form (*e.g.*, not covalently bound to a glucan), and most preferably in aglycon form. Therefore, particularly suitable cytokinins include zeatin, dihydrozeatin, kinetin, and/or N-acetylguanosine. Alternatively, or additionally, the cytokinin may also be covalently bound to a polysaccharide. In such cases, it is generally preferred that the polysaccharide preparation (*e.g.*, a beta glucan product) is enriched in the cytokinin such that the cytokinin is present in an amount of at least 0.005 wt%, more typically at least 0.05 wt%, even more typically at least at least 0.5 wt%, and most typically at least 5 wt% of

the total weight of the polysaccharide. Beta glucan was previously recognized as a polymer onto which cytokinins are immobilized to render the cytokinins in an inactive form. However, it was previously not recognized that cytokinins, and especially mixtures of cytokinins may be used to treat syndrome X, type II diabetes, improve glucose utilization, and normalize dyslipidemia.

In one particularly preferred aspect of the inventive subject matter, the cytokinin or related compound is prepared from a plant or fungus, and particularly preferred plants include various grains (*e.g.*, barley, wheat, oat, etc), various algae (*e.g.*, laminaria), various dicots (*e.g.*, soy), and preferred fungi particularly include shiitake (edodes spec.) mushrooms. Consequently, it should be recognized that contemplated dietary supplements and other food items may include a mixture of two or more of contemplated cytokinins and related compounds. Such cytokinins expressly include those in which the heterocyclic base is coupled to a sugar, and those which the heterocyclic base is not covalently coupled to a sugar.

With respect to the dietary supplement and other food item, it should be recognized that all material fit for human/animal consumption is contemplated suitable herein for combination with the cytokinins and related compounds presented herein. However, particularly preferred dietary supplements include partially purified cytokinins and related compounds that are formulated into an orally acceptable solid (*e.g.*, tablet, capsule, powder, etc.) or liquid (*e.g.*, syrup, drops, liquid extract, etc.) form. Further preferred dietary supplements and other food items include snack bars, cereals, baked goods (bread, cookies, etc.), milk products, vegetable products, etc. Such products may further include other metabolically beneficial compounds, and particularly preferred other compounds include chromium and beta glucans. With respect to the quantity of contemplated cytokinins and related compounds, it should be recognized that the amount may vary considerably. However, suitable amounts will typically be in the range of between about 1 mg of cytokinin or related compound per 100 g of food item to about 100 g of cytokinin or related compound per 100 g of food item (*e.g.*, in form of a tablet of a dietary supplement).

Therefore, the inventors specifically contemplate methods of marketing and advertising in which a product is advertised as comprising a cytokinin and/or a related compound (particularly zeatin, dihydrozeatin, kinetin, and/or N-acetylguanosine), and in which it is further advertised

that the product may have a beneficial effect (*e.g.*, protective, curative, etc.) in a person consuming that product, and especially in a person diagnosed (self-diagnosed or by medical professional) with type II diabetes, dyslipidemia, syndrome X, and/or impaired glucose utilization. For example, contemplated methods of marketing and advertising include those in which a tablet, snack bar, breakfast cereal, or plant fiber product is advertised as comprising a cytokinin or as comprising a composition enriched in cytokinins, and in which it is further advertised that the tablet, snack bar, breakfast cereal, or plant fiber product has a beneficial effect in a person consuming that product, and especially in a person diagnosed with or at risk for type II diabetes, dyslipidemia, syndrome X, and/or impaired glucose utilization. Viewed from another perspective, the inventors contemplate all manners of advertising (*e.g.*, via TV or radio ad, marketing fliers, product descriptions, typically physically associated with the product) in which cytokinins are associated with a beneficial effect in a person consuming the cytokinin, and especially in a person diagnosed with or at risk for type II diabetes, dyslipidemia, syndrome X, and/or impaired glucose utilization.

Thus, specific embodiments and applications of dietary supplements for metabolic modulation have been disclosed. It should be apparent, however, to those skilled in the art that many more modifications besides those already described are possible without departing from the inventive concepts herein. The inventive subject matter, therefore, is not to be restricted except in the spirit of the present disclosure. Moreover, in interpreting the specification, all terms should be interpreted in the broadest possible manner consistent with the context. In particular, the terms "comprises" and "comprising" should be interpreted as referring to elements, components, or steps in a non-exclusive manner, indicating that the referenced elements, components, or steps may be present, or utilized, or combined with other elements, components, or steps that are not expressly referenced.

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